DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-1213]

Environmental Assessment: Questions and Answers Regarding Drugs with Estrogenic, Androgenic, or Thyroid Activity; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity." This guidance is intended to supplement CDER's guidance for industry on "Environmental Assessment of Human Drug and Biologics Applications," issued July 1998, by addressing specific considerations for drugs that have potential estrogenic, androgenic, or thyroid pathway activity (E, A, or T activity) in environmental organisms. It is intended to help sponsors of such drugs determine whether they should submit environmental assessments (EA) for new drug applications (NDAs) and certain NDA supplements, and to clarify what information such sponsors should include if they submit a claim of categorical exclusion instead of an EA.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft

guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Raanan A. Bloom, Environmental Assessment Team, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-2185, CDER.EA.Team@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity." The National Environmental Policy Act of 1969 (Pub. L. 91-190) requires all Federal agencies to assess the environmental impact of their actions and to ensure that the interested and affected public is informed of the environmental analyses. FDA regulations at 21 CFR part 25 specify that EAs must be submitted as part of certain NDAs, abbreviated new drug applications (ANDAs), biologic license applications (BLAs), supplements

to such applications, and investigational new drug applications (INDs), and for various other actions, unless the action qualifies for a categorical exclusion. Failure to submit either an EA or a claim of categorical exclusion is sufficient grounds for FDA to refuse to file or approve an application (§ 25.15(a), 21 CFR 314.101(d)(4), and 601.2(a) and (c)).

Categorical exclusions for actions related to human drugs and biologics are listed at § 25.31. This draft guidance focuses on the categorical exclusion for actions on NDAs and NDA supplements that would increase the use of an active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment would be below 1 part per billion (1 ppb) (§ 25.31(b)). Although an action that qualifies for this exclusion ordinarily does not require an EA, FDA will require "at least an EA" if "extraordinary circumstances" indicate that the specific proposed action (e.g., the approval of the NDA) may significantly affect the quality of the human environment (§ 25.21). Research indicates that drugs with endocrine-related activity and, more specifically, drugs with E, A, or T activity have the potential to cause developmental or reproductive effects when present in the aquatic environment at concentrations below 1 ppb.[1]

FDA has, on a case-by-case basis, requested additional information from sponsors of NDAs and NDA supplements for drugs with E, A, or T activity to help it determine whether extraordinary circumstances exist. However, late cycle requests for additional environmental information have the potential to delay approval of applications. Accordingly, this guidance is intended to clarify that sponsors of drugs with potential E, A, or T activity should consult with

[1] For example, see Section II.C (pp. 7-13) of USFDA, 2013, "Response to Citizen Petition to the FDA Commissioner under the National Environmental Policy Act and Administrative Procedure Act Requesting an Amendment to an FDA Rule Regarding Human Drugs and Biologics," Docket No. FDA-2010-P-0377; U.S. Environmental Protection Agency (USEPA), Endocrine Disruptor Screening Program (EDSP), last accessed February 17, 2015, at http://www.epa.gov/endo; and Organisation for Economic Co-operation and Development (OECD), OECD Work Related to Endocrine Disrupters, last accessed February 17, 2015, at http://www.oecd.org/env/ehs/testing/oecdworkrelatedtoendocrinedisrupters.htm.

the Agency early in product development concerning the information FDA may need to determine whether an EA will be required or whether a claim of categorical exclusion will be acceptable, and what information should be included in the EA or claim of categorical exclusion.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

III. The Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in part 25 have been approved under OMB control number 0910-0322 and the collections of information in part 314 have been approved under OMB control number 0910-0001.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or http://www.regulations.gov.

Dated: April 23, 2015.

Peter Lurie,

Associate Commissioner for Public Health Strategy and Analysis.

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